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# Cost-effectiveness analysis and budgetary impact of anidulafungin treatment for patients with candidemia and other forms of invasive candidiasis in Brazil

**Cid Manso de Mello Vianna** [1], **Gabriela Bittencourt Gonzalez Mosegui** [2], **Marcus Paulo da Silva Rodrigues** [3]

## ABSTRACT

Candidemia and other forms of invasive candidiasis (C/IC) are serious conditions, especially for immunosuppressed individuals with prolonged hospitalization in intensive care units (ICU). This study analyzed the incremental cost-effectiveness and budgetary impact (BI) of treatment for IC with anidulafungin compared to amphotericin B lipid complex (ABLC) and amphotericin B deoxycholate (ABD) or conventional amphotericin B (CAB), in the Brazilian Unified Health System (SUS). A decision model was conducted with a time horizon of two weeks from the perspective of SUS. The primary effectiveness endpoints were survival and treatment response rate. All patients were followed up until successful therapy or death. BI analysis was performed based on the measured demand method. A five-year time horizon was adopted based on the number of hospitalizations (per 1,000 hospitalizations). For effectiveness measured in the successful response rate (SRR), anidulafungin dominated the ABLC and ABD formulations. In the results of the analysis with the effectiveness measured according to survival, anidulafungin had a better cost-effectiveness ratio (R$988.26/survival) compared to ABD (R$16,359.50/survival). The BI estimate related to the incorporation of anidulafungin suggests savings of approximately 148 million reais in 5 years when comparing it to ABD. The economic evaluation of anidulafungin and its comparators found it to be cost-effective. The consensus of international scientific societies recommends it as a first-line drug for IC, and its incorporation by SUS would be important.

**KEYWORDS:** Cost-benefit analysis. Anidulafungin. Candidemia. Echinocandins. Invasive candidiasis.

## INTRODUCTION

Invasive candidiasis (IC) and candidemia are infections caused by the Candida species – serious and often identified in immunocompromised patients and those with serious underlying diseases, treated in intensive care units (ICUs)[1,2], and with a mortality rate of approximately 40%[3]. In Brazil, according to the Ministry of Health (MS), there are no national data on its occurrence and extent[4]. However, Colombo *et al*.[5] analyzed data from 11 medical centers located in 9 Brazilian capital cities that identified an incidence rate of 2.49 cases of candidemia per 1,000 hospital admissions and 0.37 cases per 1,000 patients/day, a rate 2 to 15 times higher than those reported in other European countries or in the United States[4-6].

The international guidelines recommend echinocandins (caspofungin, micafungin, and anidulafungin) for the treatment of these systemic mycoses given their activity, rarity of resistance, safety profile, and better clinical results

[1]Universidade do Estado do Rio de Janeiro, Instituto de Medicina Social, Departamento de Política, Planejamento e Administração em Saúde, Rio de Janeiro, Rio de Janeiro, Brazil

[2]Universidade Federal Fluminense, Instituto de Saúde Coletiva, Departamento de Saúde e Sociedade, Niterói, Rio de Janeiro, Brazil

[3]Marinha do Brasil, Farmácia, Rio de Janeiro, Rio de Janeiro, Brazil

**Correspondence to:** Cid Manso de Mello Vianna
Universidade do Estado do Rio de Janeiro, Instituto de Medicina Social, Departamento de Política, Planejamento e Administração em Saúde, Rua São Francisco Xavier, 524, Maracan, Bloco D, 7 andar, CEP 20550-013, Rio de Janeiro, RJ, Brazil
Tel: +55 21 2334-0235

**E-mail:** cdvianna@gmail.com

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when compared to fluconazole and other medicines. As a second-line or rescue therapy, amphotericin B deoxycholate (ABD) and amphotericin B lipid complex (ABLC)[3] were used. The National Health Surveillance Agency (ANVISA) suggests anidulafungin as the first-choice treatment for candidemia, providing a loading dose of 200 mg, followed by 100 mg/day. In case of refractoriness, unavailability, or resistance, the following are recommended: one of the lipid formulations of amphotericin B, liposomal amphotericin B (LAB), at a dose of 3 mg/kg/day; or intravenous (IV) ABLC at a dose of 5 mg/kg/day. Treatment should be continued for 2 weeks after negative blood cultures and clinical improvement (usually after 5 to 7 days)[1]. In Brazil, itraconazole and ABLC are incorporated into the strategic stock of MS for the treatment of C/IC within the Brazilian Unified Health System (SUS)[7]. The direct costs associated with these diseases include the length of hospital stay, antifungal pharmacotherapy, and those related to the treatment of adverse events (AEs), which can reach US$300 million/year[8-10].

This study analyzed the incremental cost-effectiveness and budgetary impact of treatment for C/IC with anidulafungin compared to ABLC and ABD in SUS.

## MATERIALS AND METHODS

The population consisted of patients 16 years of age or older with candidiasis or other forms of C/IC determined by culture[9,11,12]. The perspective adopted was that of SUS. The time horizon of the cost-effectiveness analysis was 14 days[8,9,11] and no discount rate was applied (horizon of less than one year).

The following were used as comparators: (a) ABD or conventional amphotericin B (CAB); and (b) ABLC. The type of alternative therapy depends on the cause of discontinuation of the initial therapy[9,11]. The model outcomes were treatment success as measured by survival (SARR) and treatment response rate (SRR). The patients were followed up until therapeutic success or death[13,14]. The estimates referring to direct medical costs comprised the identification, measurement, and valuation of the resources used. The uncertainties were evaluated in the sensitivity analysis.

The treatment of C/IC was adopted as described in the Anidulafungin Recommendation Report for the treatment of patients with IC[14]: (a) anidulafungin (200 mg/IV on day 1 [D1] and 100 mg daily/IV thereafter) for one week, followed by fluconazole (400 mg – 600 mg/kg daily) IV or orally[13]; (b) ABLC at a dose of 5 mg/kg/day, once a day, for 2 weeks; and (c) ABD at a dose of 0.5 to 1.0 mg/kg IV once a day, with slow infusion for over 4 to 6 h, for 2 weeks. ABLC was used as rescue therapy for anidulafungin[1] and ABD and fluconazole for ABLC[15].

To estimate the total cost of each treatment, the daily maintenance dosages were considered. The prices were extracted from the Health Price Database (BPS)[16], and the records are from 12/21/2021 to 06/21/2022. A weighted average of the amounts paid for the quantities purchased was used. Values for the procedures, exams, and tests were obtained from SUS Procedures, Medicines, and OPM Table Management System (SIGTAP)[17]. The resources used were valued in *reais*. In-hospital treatment considered the use of the indicated medication, along with monitoring the toxic and adverse effects associated with the use of ABD and ABLC. The amount paid by SUS for 4 days of treatment is R$ 465.31. International studies[8,9,12] had important contributions to the number of queries. All the ICU patients underwent renal function tests, liver function tests, blood counts, and electrolyte tests 2–3 times a week. Table 1 shows that the costs imputed in the model are derived from the diagnosis of fungal infection, the duration of hospital treatment, hospitalization costs, the management of AEs, and drug costs, in addition to the parameters used.

The estimates of efficacy and rates of therapeutic change and other model parameters were obtained from sources listed in Table 1 and not from primary studies. All the expenses were covered by SUS. The patients remained hospitalized throughout the study period and the antifungal therapy failed only once (if the patients switched therapy after the failure of the initial therapy, the alternative therapy was considered successful)[9]. The effectiveness of ABLC was assumed to be similar to that of LAB[15,18,19].

An analytical decision model (Figure 1) was developed for the economic evaluation of the primary treatment of C/IC in patients 16 years of age or older who had candidiasis or other forms of HF using (a) anidulafungin, (b) ABLC, and (c) ABD. For the development of the model, Microsoft Excel was used. The models of Auzinger *et al.*[12], Grau *et al.*[10], Neoh *et al.*[9] and Ou *et al.*[8] served as the basis for the development of this work.

A successful IV treatment may last for 14 days. In case of failure, the therapy is changed according to the initial therapy scheme. For anidulafungin and ABD, ABLC is used in the rescue, while for ABLC, fluconazole is used in the rescue. For patients who experience clinical failure and are switched to another type of treatment, the infection is assumed to be suppressed. These subjects received an additional 14 days of second-line treatment and were followed up for 6 weeks or until death.

Budget impact analysis (BIA) was performed by comparing the use of anidulafungin with ABD in patients

**Table 1 -** Parameters and costs of the economic model

| **Procedures/Drugs/Treatments (Base case)** | **Costs (R$) (Amounts for 2022)** | | |
|---|---|---|---|
| **Drugs for pharmacotherapy** | **Unit cost** | **Daily cost** | **Source** |
| *Primary treatment — Loading dose* | | | |
| ABD 50 mg (1 mg/kg/day) | 25.21 | 35.29 | Brasil. Ministério da Saúde[16] |
| Anidulafungin 100 mg lyophilized powder (200 mg/day) | 259.49 | 518.98 | Brasil. Ministério da Saúde[16] |
| ABLC 5 mg/mL Flagon 20 mL | 569.35 | 1,992.72 | *** |
| Fluconazole 2 mg/mL (bag 100 mL) (800 mg/day) | 13.02 | 52.08 | Brasil. Ministério da Saúde[16] |
| Fluconazole 100 mg capsule | 13.79 | - | |
| *Maintenance dose* | | | |
| ABD ampoule Flagon 50 mg | 25.21 | 35.29 | Brasil. Ministério da Saúde[16] |
| Anidulafungin 100 mg/day lyophilized powder (100 mg/day) | 259.49 | 259.49 | Brasil. Ministério da Saúde[16] |
| ABLC 5 mg/mL Flagon 20 mL | 569.35 | 1,992.72 | *** |
| Fluconazole 2 mg/mL (bag 100 mL) (400 mg/day) | 13.02 | 26.04 | Brasil. Ministério da Saúde[16] |
| Fluconazole 100 mg capsule (400 mg/day) | 13.79 | 55.16 | Brasil. Ministério da Saúde[16] |
| **Hospitalization and care** | **Unit** | **Unit cost** | **Source** |
| Adult intensive care unit daily II (ICU II)* | 1 | 478.72 | Brasil. Ministério da Saúde[16] |
| Daily hospitalization for mycoses** | 1 | 224.66 | Brasil. Ministério da Saúde[16] |
| Outpatient consultation/medical consultation specialized care | 1 | 10.00 | Brasil. Ministério da Saúde[16] |
| Mycoses treatment | 1 | 116.33 | Brasil. Ministério da Saúde[16] |
| **Other hospital costs** | **(% of utilization)** | **Unit cost** | **Source** |
| | | 194.12 | Brasil. Ministério da Saúde[16] |
| Treatment of acute renal failure | | 246.89 | |
| Installation of a double lumen catheter | 80 (in ICU) | 112.48 | Brasil. Ministério da Saúde[16] |
| **Model parameters** | | | |
| **Variable** | **Measure** | | **Source** |
| **Absolute effectiveness of treatment (%)**** | | | |
| Anidulafungin | 77.49 | | Mills *et al.*[13] |
| Fluconazole | 63 | | Mills *et al*.[13] |
| ABD | 65.4 | | Mills *et al.*[13] |
| ABLC***** | 72.98 | | Mills *et al*.[13] |
| **Absolute effectiveness of treatment measured by mortality (%)** | | | |
| Anidulafungin | 20.75 | | Mills *et al*.[13] |
| Fluconazole | 28.44 | | Mills *et al*.[13] |
| ABD | 30.93 | | Mills *et al*.[13] |
| ABLC** | 39.99 | | Mills *et al*.[13] |
| **Mortality from all causes (RR)** | | | |
| Fluconazole versus ABD | 0.88 (CI 95%: 0.74 –1.05) | | Mills *et al*.[13] |
| Anidulafungin versus ABD | 1.01 (CI 95%: 0.84 –1.20) | | Mills *et al*.[13] |
| Anidulafungin versus ABLC | 1.01 (CI 95%: 0.84 –1.20) | | Mills *et al*.[13] |
| Anidulafungin versus fluconazole | 0.73 (CI 95%: 0.48 –1.10) | | Mills et al.[13] |
| IV treatment duration for successful treatment patients and their survival (days) | 14 | | Mills *et al.*[13] |

**Table 1** - Parameters and costs of the economic model (cont.)

| Model parameters | | |
|---|---|---|
| **Variable** | **Measure** | **Source** |
| **Relevant AE** | | |
| Nephrotoxicity probability for ABD (%) | 33.7 | Ou *et al*.[8] |
| Fluconazole nephrotoxicity RR compared to that of amphotericin | 0.22 (CI 95%: 0.15 –0.32) | Wang *et al*.[14] |
| Anidulafungin nephrotoxicity RR compared to that of amphotericin | 0.31 (CI 95%: 0.17 –0.57) | Wang *et al.*[14] |
| **Average therapy time** | | |
| Duration of additional hospitalization time (days) | 7 (CI 95%: 5.7 – 8.4) | Ou *et al*.[8] |
| Time needed to determine clinical failure (days) | 5 | Ou *et al*.[8] |
| Follow-up time (in weeks) | 6 | Ou *et al*.[8] |
| **Length of hospital stay in ICU (days)[a]** | | |
| Success and then survival | 7 | Ou *et al*.[8] |
| Success and then death | 7 | Ou *et al*.[8] |
| Failure and then survival | 14 | Ou *et al*.[8] |
| Failure and then death | 14 | Ou *et al*.[8] |
| Success and then survival | 23 | Ou *et al*.[8] |
| Success and then death | 23 | Ou *et al*.[8] |
| Failure and then survival | 23 | Ou *et al*.[8] |
| Failure and then death | 23 | Ou *et al*.[8] |

IV = intravenous; *R$410.92 referring to hospital services and R$67.80 to professional services; **The daily rates were calculated based on information from June 2022, using the average amount for hospitalization due to mycoses and dividing it by the average hospitalization time (R$2,246.61 in 10 days); ***ABLC 5 mg/mL – 20 mL prices, unit amount of R$569.35, and LAB 50 mg/mL – 20 mL, US$16.25 in December 7, 2021, were provided by the technical area of the SVS/MS; ICU = intensive care unit; CI = confidence interval; RR = relative risk; ****Absolute treatment efficacy and likelihood of each treatment being the best in mixed treatment comparisons using response data from confirmed infection studies; *****Approximation of LAB.

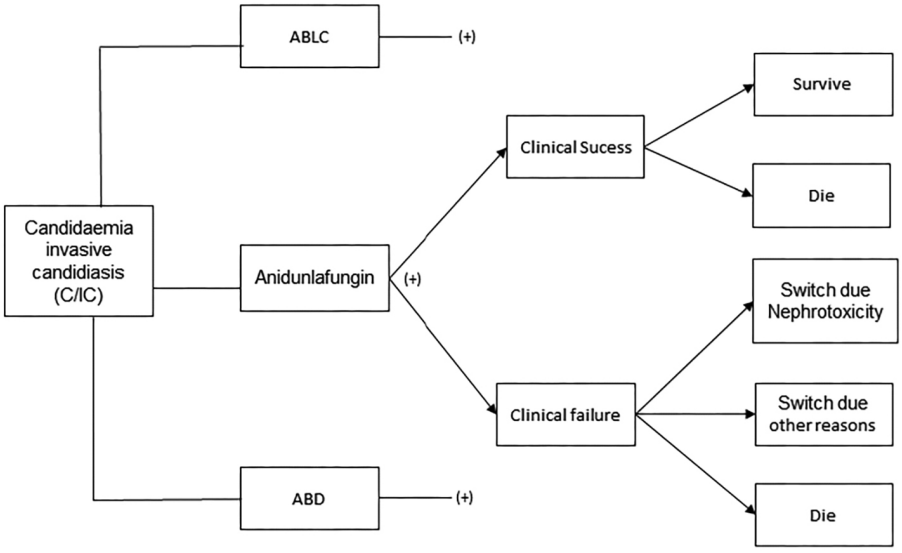


**Figure 1 -** Decision tree for the pharmacotherapeutic treatment of C/IC. Adapted from Auzinger *et al*.[12]. C/IC = Candidemia; IC = invasive candidiasis; ABLC = amphotericin B lipid complex; ABD = amphotericin B deoxycholate; (+) = treatment path.

with C/IC to assess its incorporation into SUS. The method of measured demand was used. The costs and probabilities of candidiasis, death, and survival were those of the economic assessment. According to estimates by MS,[4] the incidence of candidiasis is 18 and 135 new cases per 100,000 inhabitants, and the lowest rate was used. The perspective adopted was from SUS and the time horizon was not stipulated as its calculation is associated with the

number of hospitalizations (per 1,000 hospitalizations). Ethical approval was not required.

## RESULTS

The incremental cost-effectiveness ratio (ICER) was calculated as the ratio between the difference in direct medical costs and drug acquisition costs, and effectiveness, as the difference in the absolute response rate measured by treatment success and survival. In both alternatives, as shown in Table 2, the use of ABLC is a domination strategy, while anidulafungin has a better cost-effectiveness ratio (R$832.14/SRR). For the effectiveness measured in survival, anidulafungin has a better cost-effectiveness ratio (R$ 988.26/SARR) compared to ABD (R$ 16,359.50/SARR).

Deterministic univariate sensitivity analysis was performed, varying the absolute response rate by 10% and the probability of needing dialysis in patients with nephrotoxicity (50% for ABD)[2]. In this scenario, ABD was dominated by anidulafungin. Other scenarios did not change the cost-effectiveness ratio of anidulafungin, as shown in Table 3.

BIA points to a difference in the cost of using anidulafungin and ABD of R$100.61 (cost of treatment with anidulafungin = R$11,400.11; cost of ABD treatment = R$ 11,299.51). The additional cost to treat the entire demand in 5 years with anidulafungin would be approximately R$20 million, which has the best cost-effectiveness ratio (Table 4). As ABD was shown to be a dominating strategy with changes in the absolute response rate, probability of nephrotoxicity, and need for dialysis, BIA was estimated in these situations.

In five years, the savings in favor of anidulafungin ranged from R$80 million, when compared to the growth of dialysis, to R$150 million to reduce the absolute rate of ABD response.

## DISCUSSION

Different pharmacoeconomic analyses for these diseases and their pharmacotherapy have been performed in the international context[8-10,12], but, in the Brazilian scenario, they are nonexistent despite the fact that a public consultation on the incorporation of anidulafungin for the treatment of candidiasis is in progress.

Ou *et al*.[8] analyzed the cost-effectiveness of caspofungin, micafungin, and anidulafungin versus non-echinocandins for *C. albicans* and non-albicans Candida species. Echinocandins, especially anidulafungin, are cost-effective for IC in Taiwan. Grau *et al*.[10] compared the same echinocandins and fluconazole in the treatment of non-neutropenic adults with C/IC hospitalized in the ICU, in Spain. Anidulafungin was the most cost-effective treatment. Auzinger *et al*.[12] sought to develop a cost-effectiveness model from a UK perspective, analyzing the costs and outcomes of antifungal treatment for candidemia and IC based on the European Society of Clinical Microbiology and Infectious Disease guidelines. Anidulafungin was compared with caspofungin, micafungin, and fluconazole. The model included non-neutropenic patients aged ≥ 16 years old. Anidulafungin was cost-effective when compared to fluconazole for the treatment of C/IC, in addition to being more economical than the other echinocandins. In Australia, Neoh *et al*.[9] investigated the cost-effectiveness of anidulafungin compared to fluconazole for the treatment of IC, where anidulafungin appears as a cost-effective option.

ABLC serves as a second-line option or salvage therapy for the treatment of systemic infections in patients who are refractory or intolerant to ABD or other antifungal agents,

**Table 2 -** Incremental cost-effectiveness ratio of treatment strategies

| according to absolute response rate as measured by treatment success (SRR) | | | | | |
|---|---|---|---|---|---|
| Strategy | Costs (R$) | Δ Costs (R$) | Effectiveness (SRR) | Δ Effectiveness (SRR) | ICER (R$/SRR) |
| ABD | 11,299.51 | - | 0.654 | - | |
| Anidulafungin | 11,400.11 | 100.61 | 0.7749 | 0.12 | 832.14 |
| ABLC | 16,379.29 | 4,979.17 | 0.7298 | 0.05 | Dominated |
| according to survival absolute response rate (SARR) | | | | | |
| Strategy | Costs (R$) | Δ Costs | Effectiveness (SARR) | Δ Effectiveness (SARR) | ICER (R$/SARR) |
| ABD | 11,299.51 | - | 0.6907 | - | |
| Anidulafungin | 11,400.11 | 100.61 | 0.7925 | 0.10 | 988.26 |
| ABLC | 16,379.29 | 4,979.17 | 0.6001 | 0.19 | Dominated |

ICER = incremental cost-effectiveness ratio.

**Table 3** - Univariate deterministic analysis.

| Medication | Basal variable | Results | ICER (Δ Costs/Δ Effectiveness) |
|---|---|---|---|
| Absolute therapeutic success response rate | | | |
| Anidulafungin | 0.69741 | 12,185.39 | 7,327.39 |
| | 0.7749 | 11,400.11 | 832.14 |
| | 0.85239 | 10,614.84 | ABD dominated |
| ABD | 0.5886 | 12,179.46 | 18,623.03 |
| | 0.654 | 11,299.51 | 17,277.54 |
| | 0.7194 | 10,419.55 | 15,932.04 |
| Dialysis probability | | | |
| Anidulafungin | 0.27234 | 11,229.90 | ABD dominated |
| | 0.3026 | 11,400.11 | 832.14 |
| | 0.33286 | 11,632.18 | 2,751.58 |
| ABD | 0.27234 | 10,750.43 | 16,437.97 |
| | 0.3026 | 11,299.51 | 17,277.54 |
| | 0.33286 | 12,048.09 | ABD dominated |
| Probability of patients with an AE to develop nephrotoxicity | | | |
| ABD | 50% | 11,892.68 | ABD dominated |
| Survival absolute response rate | | | |
| Anidulafungin | 0.813 | | 820.93 |
| | 0.793 | | 988.26 |
| | 0.772 | | 1,241.27 |
| ABD | 0.722 | | 15,658.31 |
| | 0.691 | | 16,359.50 |
| | 0.660 | | 17,126.44 |

ICER = incremental cost-effectiveness ratio; ABD = amphotericin B deoxycholate; AE = adverse effects,

**Table 4 -** Budgetary impact of the use of anidulafungin against ABD and sensitivity analysis of the variation in the absolute response rate and the probability of the existence of nephrotoxicity and the use of dialysis.

| Year | Brazil, total population | IC new cases | Additional cost anidulafungin/ABD (R$) |
|---|---|---|---|
| 2022 | 214,828,540 | 38,669 | 3,890,316.19 |
| 2023 | 216,284,269 | 38,931 | 3,916,677.90 |
| 2024 | 217,684,462 | 39,183 | 3,942,033.90 |
| 2025 | 219,029,093 | 39,425 | 3,966,383.74 |
| 2026 | 220,316,530 | 39,657 | 3,989,697.85 |
| Total | - | - | 19,705,109.58 |
| Sensitivity analysis of the variation in the absolute response rate and the probability of the existence of nephrotoxicity and the use of dialysis | | | |
| Year | Answer rate (R$) | Nephrotoxicity (R$) | Dialysis (R$) |
| 2022 | –26,475,625.75 | –30,136,811.19 | –16,083,149.26 |
| 2023 | –26,655,030.85 | –30,341,025.35 | –16,192,132.48 |
| 2024 | –26,827,591.66 | –30,537,448.75 | –16,296,958.00 |
| 2025 | –26,993,304.96 | –30,726,077.74 | –16,397,623.87 |
| 2026 | –27,151,969.63 | –30,906,683.38 | –16,494,007.90 |
| Total | –134,103,522.84 | –152,648,046.41 | –81,463,871.51 |

IC = invasive candidiasis.

patients with renal failure or other contraindications[20,21]. The data leading to the approval by the Food and Drug Administration (FDA), the US regulatory agency for the clinical use of ABL, were derived from data collected from 556 cases of invasive fungal infections, through an open method in refractory or intolerant to antifungal therapy[22]. Most of these patients had been previously exposed to ABD. Another important data source is support from the Collaborative Exchange of Antifungal Research (CLEAR) sector, which provides information on the renal efficacy and safety of ABD and ABLC from data of 3,514 patients who received the drug from 1996 to 2000 in 160 US institutions[23].

However, these data have limitations: the record is retrospective; collection was based on voluntary notification, with possible selection bias; the defined response criteria were lacking; and patient follow-up was limited. In addition, because ABLC is not used in first-line treatment, no data exist on the best rescue therapy. Thus, evidence of the use of ABLC is insufficient or nonexistent. To overcome these difficulties, the existing information was assumed for ABL. This hypothesis was based on proof of the response similarity of the two formulations[18,24-29]. The model conclusions should consider this restriction.

This study also has limitations that need to be discussed. Some of them are inherent to the modeling process, which can oversimplify the progression of the disease because of divergences from the real world, the use of more than one treatment, the care and hospitalizations with the complications of the disease, and the adverse effects of the treatment. The presence of *Candida glabrata* in up to 10% of patients that prevents the use of fluconazole due to therapeutic failure was not considered[30,31]. Different international data sources served as a basis for estimating the values of transition probabilities, but, in the sensitivity analysis, such variables showed no impact on the results.

The unit costs were derived from SIGTAP and may have been underestimated. In this analysis, equal days of hospitalization were assumed for patients who used any of the technologies. The duration of admission, risk of readmission, and risk of complications could be longer, thus increasing the cost and duration of hospital care. BIA was carried out based on the product of the previous economic assessment. Consequently, all the limitations listed there also apply to this study.

## CONCLUSION

The consensus of international scientific societies recommends echinocandins, including anidulafungin, as the first-line treatment for HF and candidemia in moderately to severely ill patients. Anidulafungin proved to be a cost-effective option for the first-line treatment of HF and candidemia. More vulnerable patients would benefit from this recognized safety, tolerability, and efficacy profile, while the health system would benefit from its incorporation.

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## AUTHORS' CONTRIBUTIONS

CMMV and GBGM participated in the study design, data collection, analysis, interpretation, and the writing of the manuscript; MPSR participated in the study analysis, interpretation, and writing of the manuscript. All authors read and approved the final version.

## CONFLICT OF INTERESTS

No conflict of interests was stated by the authors.

## REFERENCES

1. Brasil. Agência Nacional de Vigilância Sanitária. Nota técnica GVIMS/GGTES/ANVISA Nº 04/2021: orientações para vigilância, identificação, prevenção e controle de infecções fúngicas invasivas em serviços de saúde no contexto da pandemia da COVID-19. [cited 2022 Dec 14]. Available from: https://www.gov.br/anvisa/pt-br/centraisdeconteudo/publicacoes/servicosdesaude/notas-tecnicas/notas-tecnicas-vigentes/nota-tecnica-04-2021-infeccoes-fungicas-e-covid19.pdf/view
2. Pappas PG, Kauffman CA, Andes DR, Clancy CJ, Marr KA, Ostrosky-Zeichner L, et al. Clinical practice guideline for the management of candidiasis: 2016 update by the Infectious Diseases Society of America. Clin Infect Dis. 2016;62:e1-50.
3. Martin-Loeches I, Antonelli M, Cuenca-Estrella M, Dimopoulos G, Einav S, De Waele JJ, et al. ESICM/ESCMID task force on practical management of invasive candidiasis in critically ill patients. Intensive Care Med. 2019;45:789-805.
4. Brasil. Ministério da Saúde. Candidíase sistêmica. [cited 2022 Dec 14]. Available from: https://www.gov.br/saude/pt-br/assuntos/saude-de-a-a-z/c/candidiase-sistemica
5. Colombo AL, Nucci M, Park BJ, Nouér SA, Arthington-Skaggs B, Matta DA, et al. Epidemiology of candidemia in Brazil: a nationwide sentinel surveillance of candidemia in eleven medical centers. J Clin Microbiol. 2006;44:2816-23.

6. Center for Disease Control and Prevention. Invasive Candidiasis statistics. [cited 2022 Dec 14]. Available from: https://www.cdc.gov/fungal/diseases/candidiasis/invasive/statistics.html
7. Brasil. Ministério da Saúde. Secretaria de Ciência, Tecnologia, Inovação e Insumos Estratégicos em Saúde. Departamento de Assistência Farmacêutica e Insumos Estratégicos. Relação nacional de medicamentos essenciais: 2022. Brasília: Ministério da Saúde; 2022. [cited 2022 Dec 14]. Available from: http://bvsms.saude.gov.br/bvs/publicacoes/relacao_nacional_medicamentos_2022.pdf
8. Ou HT, Lee TY, Chen YC, Charbonneau C. Pharmacoeconomic analysis of antifungal therapy for primary treatment of invasive candidiasis caused by Candida albicans and non-albicans Candida species. BMC Infect Dis. 2017;17:481.
9. Neoh CF, Liew D, Slavin M, Marriott D, Chen SC, Morrissey O, et al. Cost-effectiveness analysis of anidulafungin versus fluconazole for the treatment of invasive candidiasis. J Antimicrob Chemother. 2011;66:1906-15.
10. Grau S, Pozo JC, Romá E, Salavert M, Barrueta JA, Peral C, et al. Cost-effectiveness of three echinocandins and fluconazole in the treatment of candidemia and/or invasive candidiasis in nonneutropenic adult patients. Clinicoecon Outcomes Res. 2015;7:527-35.
11. Reboli AC, Rotstein C, Pappas PG, Chapman SW, Kett DH, Kumar D, et al. Anidulafungin versus Fluconazole for Invasive Candidiasis. N Engl J Med. 2007;356:2472-82.
12. Auzinger G, Playford EG, Graham CN, Knox HN, Weinstein D, Kantecki M, et al. Cost-effectiveness analysis of anidulafungin for the treatment of candidaemia and other forms of invasive candidiasis. BMC Infect Dis. 2015;15:463.
13. Mills EJ, Perri D, Cooper C, Nachega JB, Wu P, Tleyjeh I, et al. Antifungal treatment for invasive Candida infections: A mixed treatment comparison meta-analysis. Ann Clin Microbiol Antimicrob. 2009;8:23.
14. Wang JL, Chang CH, Young-Xu Y, Chan KA. Systematic review and meta-analysis of the tolerability and hepatotoxicity of antifungals in empirical and definitive therapy for invasive fungal infection. Antimicrob Agents Chemother. 2010;54:2409-19.
15. Ito JI, Hooshmand-Rad R. Treatment of Candida Infections with Amphotericin B Lipid Complex. Clin Infect Dis. 2005;40 Suppl 6:S384-91.
16. Brasil. Ministério da Saúde. Banco de preços em saúde. [cited 2022 Dec 14]. Available from: http://bps.saude.gov.br/login.jsf
17. Brasil. Ministério da Saúde. DATASUS. SIGTAP: sistema de gerenciamento da tabela de procedimentos, medicamentos e OPM do SUS. [cited 2022 Dec 14]. Available from: http://sigtap.datasus.gov.br/tabela-unificada/app/sec/procedimento/publicados/consultar
18. Leenders AC, Daenen S, Jansen RL, Hop WC, Lowenberg B, Wijermans PW, et al. Liposomal amphotericin B compared with amphotericin B deoxycholate in the treatment of documented and suspected neutropenia-associated invasive fungal infections. Br J Haematol. 1998;103:205-12.
19. Wade RL, Chaudhari P, Natoli JL, Taylor RJ, Nathanson BH, Horn DL. Nephrotoxicity and other adverse events among inpatients receiving liposomal amphotericin B or amphotericin B lipid complex. Diagn Microbiol Infect Dis. 2013;76:361-7.
20. Chandrasekar PH. Amphotericin B lipid complex: treatment of invasive fungal infections in patients refractory to or intolerant of amphotericin B deoxycholate. Ther Clin Risk Manag. 2008;4:1285-94.
21. Patterson TF, Thompson GR 3rd, Denning DW, Fishman JA, Hadley S, Herbrecht R, et al. Practice guidelines for the diagnosis and management of aspergillosis: 2016 update by the infectious diseases society of America. Clin Infect Dis. 2016;63:e1-60.
22. Walsh TJ, Hiemenz JW, Seibel NL, Perfect JR, Horwith G, Lee L, et al. Amphotericin B lipid complex for invasive fungal infections: analysis of safety and efficacy in 556 cases. Clin Infect Dis. 1998;26:1383-96.
23. Pappas PG. Amphotericin B lipid complex in the treatment of invasive fungal infections: results of the Collaborative Exchange of Antifungal Research (CLEAR), an industry-supported patient registry. Clin Infect Dis. 2005;40 Suppl 6):S379-83.
24. Falci DR, da Rosa FB, Pasqualotto AC. Comparison of nephrotoxicity associated to different lipid formulations of amphotericin B: a real-life study. Mycoses. 2015;58:104-12.
25. Herbrecht R, Natarajan-Amé S, Nivoix Y, Letscher-Bru V. The lipid formulations of amphotericin B. Expert Opin Pharmacother. 2003;4:1277-87.
26. Tiphine M, Letscher-Bru V, Herbrecht R. Amphotericin B and its new formulations: pharmacologic characteristics, clinical efficacy, and tolerability. Transpl Infect Dis. 1999;1:273-83.
27. Hamill RJ. Amphotericin B formulations: a comparative review of efficacy and toxicity. Drugs. 2013;73:919-34.
28. Kuti JL, Kotapati S, Williams P, Capitano B, Nightingale CH, Nicolau DP. Pharmacoeconomic analysis of amphotericin B lipid complex versus liposomal amphotericin B in the treatment of fungal infections. Pharmacoeconomics. 2004;22:301-10.
29. Yang H, Chaudhari P, Zhou ZY, Wu EQ, Patel C, Horn DL. Budget impact analysis of liposomal amphotericin B and amphotericin B lipid complex in the treatment of invasive fungal infections in the United States. Appl Health Econ Health Policy. 2014;12:85-93.
30. Colombo AL, Nucci M, Park BJ, Nouér SA, Arthington-Skaggs B, Matta DA, et al. Epidemiology of candidemia in Brazil: a nationwide sentinel surveillance of candidemia in eleven medical centers. J Clin Microbiol. 2006;44:2816-23.
31. Doi AM, Pignatari AC, Edmond MB, Marra AR, Camargo LF, Siqueira RA, et al. Epidemiology and microbiologic characterization of nosocomial candidemia from a Brazilian national surveillance program. PLoS One. 2016;11:e0146909.